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# THE TIME RELATIONS OF THE INFILTRATING CELLS IN ACUTE ANTERIOR POLIOMYELITIS \*

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The various phases of poliomyelitis have been studied in the human subject, and experimentally in animals. Investigations reported from the laboratories of Rockefeller Institute are notable. Comparatively recent and very complete is the work done by the committee of investigation on the New York epidemic of 1907, and also that directed by the Massachusetts state board of health in 1910 and 1911.

My work has had for its special object the determination of the time at which the different types of infiltrating cells are most evident in the lesions of the spinal cord. Material was available from 2 sets of experiments on monkeys, experiments in which the time of inoculation, and of onset of symptoms (in the greater number) were recorded. Twenty-two cases of the series were in animals used by Dr. H. J. Rosenau, and an additional 17 cases in animals used for work on poliomyelitis by Dr. H. C. Low of Boston.

The animals of the 1st group were infected by subdural injection of an emulsion of the virus contained in the spinal cord of monkeys that had died of poliomyelitis. Those of the 2nd group were injected variously—with emulsion of the spinal cord of human poliomyelitis, with material from the nasal mucous membrane of patients during the disease, and with Emulsion M. A. (Flexner and Lewis). Regardless of the different sources of the virus, similar results were obtained in all cases.

All blocks of tissue were primarily fixed in Zenker's solution and stained by the eosin methylene-blue method, after embedding in paraffin.

In the set of 21 cases in which the exact time of infection, of onset of symptoms, and of death was known, the periods were as follows:

Average length of time from infection until death.....	8-9 days
Average length of incubation period.....	4-5 days
Average time of duration of symptoms (until death).....	4 days

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The variation in each of these periods was rather wide. The shortest time between infection and death was 4 days, the longest 30 days. The shortest incubation period was 2 days, the longest 17 days. The shortest duration of symptoms before death was 1 day, the longest 24 days.

The cords showed different combinations of those lesions usually found in poliomyelitis—engorgement of the capillaries, and small perivascular hemorrhages in the gray substance. This was not an early manifestation in all instances, as these findings existed in one case in which the symptoms had persisted for 24 days. Occasional pial infiltration was seen, and perivascular dilatation with and without the presence of infiltrating cells.

Cell-infiltration existed to some extent in all sections, but it varied widely in type and degree. Three kinds of cells were distinguished: small mononuclear (lymphoid) cells, polymorphonuclear leukocytes, and large cells of the endothelioid type, frequently found where phagocytosis takes place. Sometimes all three were grouped together with slight predominance of one over the other; in other instances polymorphonuclear cells appeared almost exclusively; again, few, if any, polymorphonuclear cells were discovered among the many small mononuclear cells. It is almost always true that some polymorphonuclear leukocytes occur in sections containing the large endothelioid type of cell.

In regard to the relation of the character of the infiltrating cells to the incubation period, and the duration of symptoms, it seems to be generally true that the polymorphonuclear cells are an early manifestation, tho they may endure for some time, as was shown clearly by the fact that in those cases which developed symptoms 2 or 3 days after inoculation, many polymorphonuclear cells were found in connection with extreme degeneration of the anterior-horn cells. Their relation to these cells was not only pericellular, but also very apparently intracellular, a condition that has been previously noted by others.

The case with the shortest incubation period (2 days) in the series, in which death followed 3 days later, exhibited the infiltrating cells as a combination of small round cells and polymorphonuclear cells, with a few cells of the endothelioid type, together with extreme degeneration of the ganglion cells of the anterior horns. In direct contrast, both as to time and type of cell, was a case in which the animal lived 24 days after the onset of symptoms 6 days after inoculation. In this case the infiltrating cells were mainly small mononuclears, appearing with

extreme degeneration of the anterior-horn cells. From the sections examined the presence of polymorphonuclear cells was established to be, within certain limits, uniform with the destruction of the anterior-horn cells, the brief incubation period, and short duration of the disease followed by death. In other words, the condition apparently is governed by the toxicity of the infecting agent.

This finding was further emphasized by examination of the 17 additional cases, all showing results that corresponded in general with those of the preceding group. In these later cases, however, the average duration of symptoms, followed by death, was 26.5 days, in comparison with the 8 or 9-day period, as noted in the foregoing. The variation here, too, ranged from 96 to 6 days. This group of cases was definitely divided into 2 classes: one of long, and one of short duration. The longer varied from 17 to 96 days, the shorter from 6 to 11 days, thus coinciding with the previously described set. In all the cases of long duration, the infiltrating cells were few, with varying degrees of cell-destruction, tho never so extreme as in the 1st group. Distinct history of paralysis, however, puts them undoubtedly in the series. The group of short duration, on the other hand, shows changes wholly comparable with those of the 1st group. The infiltrating cells were a combination of the small round cells and polymorphonuclear cells, with a moderate to extreme loss of nerve cells in the anterior horns, the relation between the two varying exactly with the duration of symptoms before death.

Strauss, in his otherwise complete discussion of the histopathology of acute poliomyelitis, in the report of the New York state commission, leaves unanswered the question of the real presence of polymorphonuclear leukocytes in the cord. In my study certainly many atypical cells of variously shaped nuclei were to be found in the anterior horns, in the interstitial tissue, but they were not difficult to distinguish from the definite and easily recognizable polymorphonuclear type. They also differed distinctly from any form of proliferated glia cell which I have encountered in any instance of glia-cell increase. Morphology and staining reaction left no doubt as to their identification. The only element of difference is that Strauss worked with human material. The one human case recently at the disposal of this laboratory—one of short duration and very acute clinical history—presented a picture very similar to that of the animal cases.

One very prominent point to be noted concerning the infiltrating cells found in the cord in acute anterior poliomyelitis, was the difference between the cells about the blood-vessels and those surrounding the

degenerating anterior-horn cells. The cells about the blood-vessels in the series here considered, were almost exclusively of the small mononuclear type, even in cases where polymorphonuclear cells predominated in the anterior horns.

#### SUMMARY

Thirty-eight cases were examined, all in monkeys.

The material examined was fixed in Zenker's fluid and stained with the eosin methylene-blue stain according to Mallory.

All cases showed the usual findings in acute anterior poliomyelitis.

Cases with a short incubation period and brief duration before death, showed a corresponding abundance of polymorphonuclear cells in the pericellular infiltrate, and an extreme degeneration of anterior-horn nerve cells.

Cases in which death was delayed weeks or months showed a persistence of small round-cell infiltration, but no polymorphonuclear leukocytes, even in cases with extreme nerve-cell destruction.

#### CONCLUSIONS

The duration of the disease, the incubation period, and the cell degeneration in acute anterior poliomyelitis, apparently depend on the virulence of the infecting virus.

The polymorphonuclear leukocytes disappear after a time (in the cases here considered apparently within 3 weeks), but the small mononuclear cells, when death is sufficiently delayed, persist.